REMARKS

Claims 1-3, 6-29 and 33 are pending herein. By the Office Action, claims 1-25 are rejected under 35 U.S.C. §112, second paragraph, §102, and §103. The Office Action has also objected to the arrangement of the specification. By this Amendment, claims 1-3 and 6-29 are amended, claims 4, 5 and 30-32 are canceled, and new claim 33 is added.

The attached Appendix includes marked-up copies of each rewritten paragraph (37 C.F.R. §1.121(b)(1)(iii)) and claim (37 C.F.R. §1.121(c)(1)(ii)).

I. Drawings

The Office Action indicates that the drawings originally submitted are informal, but are acceptable for examination purposes only. Applicants acknowledge that formal drawings will be submitted at the appropriate time.

II. Specification

The specification is objected to for the non-standard arrangement. Applicants have reorganized the specification according to the guidelines provided by the Examiner. Thus, applicants submit that the objection to the specification is obviated. Reconsideration and withdrawal of this objection are respectfully requested.

III. Information Disclosure Statement

The Office Action returned to Applicants copies of their Forms PTO-1449 previously filed with an Information Disclosure Statement. However, not all of the references have been initialed by the Examiner to indicate that the references have been considered of record.

Specifically, the Office Action indicates that the French reference 2 268 818, crossed-out on the Form, will not be considered in the absence of either an English translation or a statement of relevancy therefor. However, under 37 C.F.R. 1.98 (a)(3), Applicants have complied with the requirements for submission of an Information Disclosure Statement, and all of the cited references must be considered of record by the Examiner. The reference in

question was cited by a foreign patent office in a counterpart foreign application. Both an original copy and an English version of the foreign search report were included with the Information Disclosure Statement. The citation of the reference in the foreign search report constitutes the concise statement of relevance of the reference, as understood by the Applicants, required by MPEP §609 A(3). Accordingly, an English language translation of the reference is not required, and the reference must be considered by the Examiner.

The Examiner is thus respectfully requested to consider the remaining reference of record, and accordingly, initial and return to the undersigned a copy of the subject Form PTO-1449. For the convenience of the Examiner, a copy of the form is attached.

IV. Rejections under §112, second paragraph

Claims 1-25 are rejected under 35 U.S.C. 112, second paragraph, for allegedly being indefinite. Without admitting to the propriety of the rejection and solely to expedite prosecution, Applicants have amended the pending claims, where applicable, to overcome this rejection without narrowing the claims.

The Office Action alleges that claim 1 is indefinite because the structural relationship between the "complex" and "complexing groups" is unclear. Applicants respectfully traverse this aspect of the rejection. The "complex" is unambiguously indicated in the claim as the combination of the capture phase and the target biological material. The "complexing groups" of the first or second complexing groups are those that are bound to a hydrophilic polymer and also bound to a transition metal by a coordinate bond. The specification indicates that such complexing groups may be derived from itaconic acid or maleic acid-co-methyl vinyl ether (see page 5, lines 1-3; page 8, lines 30-35). According to the invention, the complexing groups are used to functionalize the hydrophilic polymer (see Examples 2 and 3, 2)). In addition, the complexing groups are selected to interact with the transition metal (see Examples 3, 2) and 4).

The Office Action further alleges that the term "coordinated" in claim 1 is indefinite. Applicants submit that the term "coordinated" is not indefinite. A coordinate bond is a type of covalent bond where a pair of electrons are donated by only one of the two atoms that are joined by the bond (see Hawley's Condensed Chemical Dictionary, 13th Ed., 1997, p. 296, copy attached). Thus, any person skilled in the art would understand the meaning of the term "coordinated."

The Office Action alleges that the Markush group recited in claim 21, which is recited in amended claim 28, is indefinite because the group contains both label components and binding components. Applicants respectfully traverse this aspect of the rejection. Claim 28 is amended to clarify that the recited marker comprises a material selected from the group, and to clarify that the recited members can be part of the marker. Because all of the recited members can be marker components, the members possess at least one property in common which is mainly responsible for their function in the claimed relationship, and it is clear from their very nature that all of them possess this property. See, MPEP 2173.05(h)(I).

In view of the above amendments and remarks, Applicants submit that the rejection is overcome. Reconsideration and withdrawal of the rejection are requested.

V. Rejections under §102

Claims 1-8, 10-12, 14-15, and 17-25 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Nowinski et al., US 4,843,010. Applicants respectfully traverse this rejection, insofar as the rejection is applicable to the pending claims.

The Office Action cites Nowinski et al. for disclosing a method for isolating a target analyte, wherein the capture phase consists of a conjugate polymerizable organic monomer/reactant and a conjugate reporter/reactant. The reactant of the monomer/reactant conjugate is preferably an antibody or an antigen, but may also be other biological agents having specificity for a target analyte (see col. 6, lines 45-54). A complex is formed between

the monomer/reactant conjugate and target analyte. A conjugate reporter/reactant is required as the detection phase (see col.8, lines 63-64). The reactant of the conjugate reporter/reactant prefereably recognizes a different portion of the analyte and binds in a manner that does not interfere with the binding of the reactant of the conjugate monomer/reactant.

The conjugate monomer and conjugate reporter and the analyte are mixed to obtain a labeled complex. Once the analyte is bound to the monomer/reactant conjugate, the complex can be separated from the other assay components by polymerizing the monomer/reactant conjugate bound to the analyte. Nowinski describes the addition of additional non-derivatized monomer and the initiation of polymerization, which yields a copolymer of non-derivatized monomer with the monomer/reactant conjugate (see col. 10, lines 39-44).

According to Nowinski, transition metals may be used to initiate the photopolymerization of certain monomers (see col. 9, lines 57-65). It should be appreciated that since these transition metals serve to initiate polymerization of the monomer, the transition metal will, at most, be present only at the ends of the resulting polymer.

The transition metal of the claimed invention, in contrast, forms a coordinate covalent bond with the complex group attached to the hydrophilic polymer, hence the complexing groups are "coordinated by a first transition metal, which is chelated to a first biological species...." Thus, according to the claims, the transition metal forms a constitutive element of the capture phase. Although Nowinski describes the initiation of photopolymerization using transition metals, the transition metal does not interact with, nor is it bound to, the reactant portion of the detection phase described by the reference. At most, the transition metal may be present in the polymer described by Nowinski at either end of the polymer chain only as an initiator residue.

Further, it should be noted that the transition metal of the claimed invention also contributes to the specificity of the process, because the transition metal interacts with the biological material (see page 5 lines 26-33 in the specification). In instances where the capture phase and/or the detection phase comprises a magnetic compound (page 4, lines 28-30), the magnetic compound does not become linked to the biological material. Thus, the magnetic compound, when present, has a different function from that of the transition metal.

Therefore, Nowinski fails to teach each and every feature of the claimed invention because the process disclosed by Nowinski requires a separate polymerization step. In addition, the capture phase disclosed by the reference is structurally different from the claimed invention because it does not incorporate the transition metal. Thus, the reference does not anticipate the claims. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1-5, 8-15, 17, and 19-25 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Rohr et al., US 5,445,971. Applicants respectfully traverse this rejection, insofar as the rejection is applicable to the pending claims.

The Office Action cites Rohr et al. for allegedly disclosing a process for isolating a target material using a solid phase reagent as a capture phase and a magnetically-labeled reagent as a detection phase. The capture phase described by Rohr consists of a binding member attached to a solid phase, wherein the binding member is capable of directly or indirectly binding the analyte. In the case of indirect binding, the binding member is linked to an ancillary binding member. The binding member is a biological material (see, col. 5, lines 14-44) having specific affinity with the analyte (see col. 5, line 45 to col. 6, line 22).

In particular, the Office Action refers to Table 1, and alleges that the reference discloses a "capture phase has a core comprising polystyrene or polyacrylate material with a transition metal layer." However, the reference clearly indicates that Table 1 describes

materials suitable for the magnetic label, or the detection phase of the process (see col. 9, line 35 to col. 10, line 27). Thus, Rohr clearly indicates that the magnetic particles are not incorporated into the solid phase material, which serves as the capture phase upon which the complex of the magnetically label and the analyte is immobilized (see col. 3, lines 19-39). Thus, the portion of the reference cited in the Office Action clearly has no bearing on the capture phase of the claimed invention. As discussed above with respect to Nowinski, the transition metal of the claimed invention also contributes to the specificity of the process, and does not merely serve as a magnetic label, as disclosed by Rohr.

To the extent that the teachings of the reference relate to the detection phase of the claimed invention, the portion of Table 1 indicates that the magnetic cores are coated with a non-magnetic material. Thus, the magnetic material is not bound to the biological material because of the intervening non-magnetic polymer layer. In contrast, in the detection phase of the claimed invention, the transition metal is directly linked to the biological material.

Thus, Rohr does not anticipate the claimed invention because it does not disclose each and every feature of the claimed invention. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1-5, 9, 10-12, 15, 17, and 19-21 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Owen et al., US 5,866,099. Applicants respectfully traverse this rejection, insofar as the rejection is applicable to the pending claims.

The Office Action has cites Owen et al. for disclosing a method of isolating a target substance using a capture phase that comprises magnetic-polymer particles, which consist of magnetic particles on the surface of which the target substance is linked, through at least one bifunctional agent. The polymer is associated with the metal via coordination, but said metal is not directly linked to the target substance. In contrast, in the claimed invention, the metal is directly linked to the biological material. Thus, as previously discussed with respect to

Nowinski, the transition metal of the claimed invention contributes to the specificity of the process, because the transition metal interacts directly with the biological material. In Owen, however, the transition metal does not interact with the biological material.

Thus, because Owen does not teach or suggest the direct linkage of the transition metal to the biological material, the reference fails to teach each and every limitation of the claims. Therefore, Owen does not anticipate the claimed invention. Reconsideration and withdrawal of the rejection are respectfully requested.

VI. Rejections under §103

Claims 6-7 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Rohr et al. or Owen et al. in view of Schaeffer et al., US 4,784,912. Applicants respectfully traverse this rejection, insofar as the rejection is applicable to the pending claims.

Rohr and Owen are applied as cited in the rejections under §102(b). The combined references fail to teach or suggest the use of N-isopropylacrylamide as the water-soluble monomer that is incorporated into the capture phase or polymer particles.

To cure this deficiency in the teachings of Rohr and Owen, the Office Action cites Schaeffer, which teaches polymeric latex particles incorporating units of hydrophilic or water-soluble polymerizable monmers, including acrylamide, methacrylamide, and N-isopropylacrylamide. At best, the combination of Rohr and Owen, taken in view of Schaeffer, would only yield the linkage of a transition metal to the latex particle taught by Schaeffer. The addition of Schaeffer fails to cure the above-described deficiencies of Rohr and Owen, because the combined teachings of the references still fail to teach or suggest the direct linkage of the transition metal to the biological material.

Thus, for at least these reasons, claims 6-7 would not have been obvious over the cited references. Reconsideration and withdrawal of the rejection are respectfully requested.

Claim 16 is rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Nowinski or Rohr in view of Ohdaira et al. Applicants respectfully traverse this rejection, insofar as the rejection is applicable to the pending claims.

Nowinski and Rohr are applied as cited in the rejections under §102(b). The combined references fail to teach or suggest that functional monomers include complexing groups derived specifically from itaconic acid or maleic anhydride-co-methyl vinyl ether.

To cure this deficiency in the teachings of Nowinski and Rohr, the Office Action cites Ohdaira, which teaches polymeric latex particles incorporating copolymers of ethylene and an α,β-ethylenically unsaturated carboxylic acid and further having an aromatic vinyl compound grafted thereto. The α,β-ethylenically unsaturated carboxylic acid is at least one of itaconic acid and maleic acid. Although the reference suggests that the particle may be chemically bonded to an antigen or antibody, the combination of Nowinski and Rohr, taken in view of Ohdaira, still would not teach or suggest the linkage of the transition metal to the antigen or antibody. Since none of the cited references teach or suggest the direct linkage of the transition metal to the biological material, Ohdaira fails to cure deficiencies of Nowinski and Rohr.

Thus, for at least these reasons, claim 16 would not have been obvious over the cited references. Reconsideration and withdrawal of the rejection are respectfully requested.

VII. References Cited

In the Notice of References Cited (PTO-892) enclosed with the Office Action, the Adamczyk et al. patent is identified by the patent number 5,489,080. This appears to be the incorrect patent number, as the reference is identified using 5,459,080 in the Office Action and the 5,489,080 patent is issued to Allen. Applicants respectfully request that the Examiner issue a corrected copy of the Form 892 that indicates the correct patent number (5,459,080) for Adamczyk et al.

VIII. Conclusion

In view of the foregoing remarks, Applicants respectfully submit that the application is in condition for allowance. Favorable consideration and prompt allowance of claims 1-3, 6-29 and 33 are respectfully requested.

Should the Examiner believe that anything further would be desirable in order to place the application in better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below.

Respectfully submitted,

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WPB/SXT:amw

Attachment:
Appendix
Form PTO-1449
Translation of Annexes to IPER
Preliminary Amendment

Date: March 25, 2002

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Telephone: (703) 836-6400

DEPOSIT ACCOUNT USE AUTHORIZATION
Please grant any extension necessary for entry;
Charge any fee due to our Deposit Account No. 15-0461

APPENDIX

Changes to Specification:

Page 1, between lines 2 and 3 insert the headings:

BACKGROUND OF THE INVENTION

1. Field of the Invention

Page 1, between lines 11 and 12 insert the headings:

2. Description of Related Art

Page 1, lines 12-23, delete current paragraphs.

Page 2, between lines 17-18, insert new headings and paragraphs as follow:

SUMMARY OF THE INVENTION

In the presentation of the invention which follows, reference is made in particular to the isolation of a target protein biological material, but, needless to say, the scope of the invention should not be limited thereto.

Thus, according to the invention, the expression "biological material" means, in particular, a protein or glycoprotein material such as an antigen, a hapten, an antibody, a protein, a peptide, an enzyme or a substrate, and fragments thereof; but also a nucleic material such as a nucleic acid (DNA or RNA), a nucleic acid fragment, a probe or a primer; a hormone.

DETAILED DESCRIPTION OF THE INVENTION

Changes to Claims:

Claims 4, 5 and 30-32 are canceled.

Claim 33 is added.

The following is a marked-up version of the amended claim:

1. (Amended) ~~Process~~ A process for isolating a target biological material contained in a sample, comprising: ~~according to which a capture phase is provided, said~~ contacting said target biological material ~~is placed in contact~~ with at least ~~the~~ a capture phase~~material~~, and

detecting ~~the~~ a complex of said capture phase and ~~/~~said target biological material~~complex is detected~~,

wherein the capture phase of said process ~~being characterized in that,~~ ~~the capture phase is in microparticulate or linear form and~~ consists of at least one first ~~particulate or linear~~ hydrophilic polymer, ~~with a hydrophilic apparent nature~~ and first complexing groups, these groups being ~~linked~~ covalently bound to said first hydrophilic polymer and ~~by~~ coordinated~~tion~~ by a first transition metal, which is ~~itself linked by chelation~~chelated to a first biological species ~~capable of specifically recognizing~~having specific affinity to the target biological material.

2. (Amended) ~~Process~~ The process according to Claim 1, ~~characterized in that~~wherein the capture phase comprises a marker ~~in order to obtain~~for use as a detection phase for detecting said biological material.

3. (Amended) ~~Process~~ The process according to Claim ~~1~~2, ~~characterized in that~~wherein the ~~a~~ detection phase ~~is also provided, which is in microparticulate or linear form and~~ consists of ~~at least one~~ a second ~~particulate or~~ hydrophilic ~~linear~~ polymer, ~~of hydrophilic apparent nature,~~ and second complexing groups, ~~these groups being~~which are ~~linked by coordination~~ coordinated to a second transition metal, which is ~~itself~~ linked to a second biological species ~~capable of specifically recognizing~~having specific affinity to the target biological material, and a marker.

6. (Amended) ~~Process~~ The process according to Claim 41, ~~characterized in that~~wherein the first hydrophilic polymer is a functionalized polymer obtained by

polymerization of a water-soluble monomer, of an acrylamide, of an acrylamide derivative, of a methacrylamide or of a methacrylamide derivative, ~~of~~ having at least one crosslinking agent and ~~of~~at least one functional monomer.

7. (Amended) ~~Process~~ The process according to Claim ~~5~~3, ~~characterized in that~~wherein the second hydrophilic polymer is a functionalized polymer obtained by polymerization of a water-soluble monomer, of an acrylamide, of an acrylamide derivative, of a methacrylamide or of a methacrylamide derivative, ~~of~~ having at least one crosslinking agent and ~~of~~ at least one functional monomer.

8. (Amended) ~~Process~~ The process according to Claim 6, wherein~~characterized in that~~ the water-soluble monomer is ~~chosen~~ selected from the group consisting of N-isopropylacrylamide, N-ethylmethacrylamide, N-n-propylacrylamide, N-n-propylmethacrylamide, N-n-isopropylmethacrylamide, N-cyclopropylacrylamide, N,N-diethylacrylamide, N-methyl-N-isopropylacrylamide and N-methyl-N-n-propylacrylamide~~, the monomer preferably being N-isopropylacrylamide (NIPAM)~~.

9. (Amended) ~~Process~~ The process according to Claim 6, ~~characterized in that~~wherein the functional monomer corresponds to formula I below:

$CH_2=C(Z)-(X)_m-(R)_p-(Y)_n$ (I)

wherein: Z represents H, a C1-C5 alkyl radical or a benzyl, -COOH or -CO-NH-$CH(CH_3)_2$ radical,

Y represents -CH_2-COOH, -$N(CH_2$-$COOH)_2$, -N(CH-COOH) -N(CH-COOH) (CH_2-COOH), or -$N(CH_2$-CH_2-$NH_2)_2$
|
(CH_2-COOH)

X represents -$NH(CH_2$-CH_2-), --$N(CH_2$-CH_2-$)_2$, -$N(CH_2$-COOH) (CH_2-CH_2-), or CH(COOH)-,

R represents a linear hydrocarbon-based chain, optionally interrupted with at least one hetero atom such as O or N,

m and p are each an integer which, independently of each other, are equal to 0 or 1, and

n is an integer ranging between 1 and 3.

10. (Amended) ~~Process~~ The process according to Claim 9, ~~characterized in that~~wherein the functional monomer is chosen from carboxylic derivatives, optionally containing nitrogen, itaconic acid, acrylic derivatives and methacrylic derivatives.

11. (Amended) ~~Process~~ The process according to Claim 1, ~~characterized in that~~wherein the capture phase is in microparticulate form and ~~in that~~ the average particle size is not more than 5 μm.

12. (Amended) ~~Process~~The process according to Claim 3, ~~characterized in that~~wherein the detection phase is in microparticulate form and ~~in that~~ the average particle size is not more than 5 μm.

13. (Amended) ~~Process~~ The process according to Claim 1, ~~characterized in that~~wherein the capture phase also comprises a flat or particulate support.

14. (Amended) ~~Process~~ The process according to Claim 13, ~~characterized in that~~wherein the support is particulate and consists of an organic or inorganic, hydrophilic or hydrophobic core.

15. (Amended) ~~Process~~ The process according to Claim 14, ~~characterized in that~~wherein said core is ~~chosen~~ selected from the group ~~comprising~~ consisting of polystyrene, silica and metal oxides.

16. (Amended) ~~Process~~ The process according to Claim 14, ~~characterized in that~~wherein said core also contains a magnetic compound.

17. (Amended) ~~Process~~ The process according to Claim 14, ~~characterized in that~~wherein said core is coated with said first hydrophilic polymer, the ~~latter~~ first hydrophilic polymer being linear.

18. (Amended) ~~Process~~ The process according to Claim 14, ~~characterized in that~~ wherein said core is coated with said first hydrophilic polymer, said first hydrophilic polymer being particulate.

19. (Amended) ~~Process~~ The process according to Claim 1, ~~characterized in that~~wherein the first hydrophilic polymer is poly(N-isopropylacrylamide) and the complexing groups are derived from itaconic acid or from maleic anhydride-co-methyl vinyl ether.

20. (Amended) ~~Process~~ The process according to Claim 3, wherein~~characterized in that~~ the second hydrophilic polymer is poly(N-isopropylacrylamide) and the complexing groups are derived from itaconic acid or from maleic anhydride-co-methyl vinyl ether.

21. (Amended) ~~Process~~ The process according to Claim 1, wherein~~characterized in that~~ the first transition metal is ~~chosen~~ selected from the group consisting of zinc, nickel, copper, cobalt, iron, magnesium, manganese, lead, palladium, platinum and gold.

22. (Amended) ~~Process~~ The process according to Claim 3, wherein~~characterized in that~~ the second transition metal is ~~chosen~~ selected from the group consisting of zinc, nickel, copper, cobalt, iron, magnesium, manganese, lead, palladium, platinum and gold.

23. (Amended) ~~Process~~ The process according to Claim 1, wherein~~characterized in that~~ the ~~placing in contact~~ contacting of the first biological species with the capture phase is carried out at a pH above or equal to the isoelectric point of said first biological species.

24. (Amended) ~~Process~~ The process according to Claim 3, wherein~~characterized in that~~ the ~~placing in contact~~contacting of the second biological species with the detection phase is carried out at a pH above or equal to the isoelectric point of said second biological species.

25. (Amended) ~~Process~~ The process according to Claim 1, wherein~~characterized in that~~ the first biological species is rich in at least one of histidine and/~~or~~ cysteine.

26. (Amended) ~~Process~~ The process according to Claim 3, ~~characterized in that~~ wherein the second biological species is rich in at least one of histidine and/~~or in~~ cysteine.

27. (Amended) ~~Process~~ The process according to Claim 1, ~~characterized in that~~wherein an agglutination reaction is used.

28. (Amended) ~~Process~~ The process according to Claim 2, ~~characterized in that~~wherein the marker for the detection phase ~~is chosen~~ comprises a material selected from the group consisting of an enzyme, biotin, iminobiotin, a fluorescent component, a radioactive component, a chemiluminescent component, an electron-density component, a magnetic component, an antigen, a hapten and an antibody.

29. (Amended) ~~Process~~ The process according to Claim 2, ~~characterized in that~~ wherein the enzyme linked immonosorbent assay (ELISA) technique is used.